Remarks

Upon entry of the foregoing claim amendments, claims 1, 4, 6-16, and 21-22 are pending in the application. Claims 1, 4, 8, 9, 13-16, 21, and 22 have been amended to clarify the subject matter contained therein. The amendments and new claims do not introduce any new subject matter within the meaning of 35 U.S.C. §132. Therefore, entry of the amendments is respectfully requested.

1. Claim Objections

The Official Action states that claims 3, 13, 18 and 20 are objected to based on various typographical errors.

Applicants have amended and cancelled claims in response to the cited objections. Applicants respectfully submit the claims are now in compliance, and the objections are moot. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw these objections and allow the pending claims to proceed to grant.

2. Rejection of claims 8, 14-16, 18, and 20-22 under 35 U.S.C §112

The Official Action states that claims 8, 14-16, 18, and 20-22 are rejected under 35 U.S.C. 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Official Action states the following:

> Claim 8 recites "particularly", and it is unclear whether it is the only linear peptide of the claim, or whether it is merely exemplary of the subgenus 'linear peptides', and thus the claim is indefinite.
>
> Claim 14 recites, "can be administered orally and intravenously", and it is unclear whether the compound is administered orally or intravenously or whether it must be administered both orally and intravenously or whether it is merely optional that it need only be

capable of being administered orally and intravenously, and thus the claim is indefinite.

Claim 15 recites "is used in a quantity", which is unclear as to how exactly the antagonist is "used". It is unclear whether the antagonist is 'used' to make a tablet, 'used' as a binder, or whether it is administered at a dose of 0.1 to 50 mg/kg /day, and thus the claim is indefinite.

Claims 16, 21 and 22 recite "medicament intended for administration in a quantity of 1 to 75, 5 to 50, and 5 to 25 wt.%, respectively, and it is unclear what the is weight %. Weight % is a relative term, requiring a benchmark for comparison, and it is unclear whether the wt.% is of the composition or of the patient, and thus the claims are indefinite.

Claims 18 and 20 depend from cancelled claims, and it is unclear as to what is being claimed, and therefore the claims are indefinite.

RESPONSE

Applicants have amended the claims in response to the above cited rejections. Applicants believe that the claim amendments overcome the bases of the rejections, thereby rendering the rejections moot. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection and allow the pending claims to proceed to grant.

3. Rejection of claims 1-6, 9, 12-16, 21, and 22 under 35 U.S.C. §103(a)

The Official Action states that claims 1-6, 9, 12-16, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable

over Foulon (WO 97/15556 A1, reference A6: PTO-1449, 8/11/2005), in view of Serradeil-Le Gal (reference A15: PTO-1449, 8/11/2005). The Official Action also states that in the interest of compact prosecution, U.S. Patent 5,994,350, the U.S. National Stage filing of WO 97/15556 A1, is relied upon as the English equivalent.

In particular, the Official Action states the following:

> The instant claims are drawn to treating "disturbances or illnesses of an inner ear comprising administering at least one vasopressin receptor antagonist" to a patient in need. The elected species administered is known in the art as SR 121463A (e.g. page 2730, reference A15: PTO-1449, 8/11/2005).
>
> Foulon teaches SR 121463A1 as the compound (claim 6, column 52, lines 59-61), as a pharmaceutical composition alone (claim 13) and in combination with irbesartan (claim 17, note Certificate of Correction sheet to amend the compound of claim 17), and a method "for the treatment of diseases in which the vasopressin and/or oxytocin receptor is involved which comprises administering to a patient in need of such treatment an effective amount of a compound according to claim 6" (claim 23).
>
> Foulon teaches that, "The compositions according to the invention can also be used in the treatment of Meniere's syndrome..." (column 24, lines 61-64) and that the pharmaceutical compositions of the present invention for various routes of administration, including oral or intravenous administration, "the active principles of formula (1) [the genus of the elected species], or their possible salts, solvates or hydrates can be administered as unit administration formulations, as a mixture with conventional pharmaceutical vehicles, to animals and to man" (column 23, lines 34-41). Additionally, "each unit dose can contain from 0.5 to 1000 mg, preferably from 1 to 500

mg, of active ingredients in combination with a pharmaceutical vehicle." (column 23, lines 54-56) and that, "In order to obtain the desired prophylactic or therapeutic effect, the dose of active principle can vary between 0.01 and 50 mg per kg of body weight per day." (column 23, lines 51-53).

It is noted that the instant specification states that Meniere's disease is "normally associated with the symptoms vertigo, impairment of hearing and tinnitus aurium" (page 4, specification). The art recognizes that the hearing impairment is low frequency hearing loss ("deep sound" as claimed) and that Meniere's disease is "linked" with endolymphatic hydrops.

Serradeil-Le Gal teaches SR 121463A, the elected species as the fumarate salt (e.g. page 2730, *Materials)*.

The difference between that which is claimed, and that which is taught by Foulon, is that while Foulon teaches administering SR 121463A to treat diseases in which vasopressin receptor is involved, and that Meniere's syndrome is one such disease, Foulon does not teach treating Meniere's disease with SR 121463A.

It would have been obvious to treat Meniere's disease with SR 121463A, and thus treat a disturbance or illness of the inner ear associated with vertigo, low frequency hearing impairment, tinnitus, and hydrops, as Foulon teaches that one could treat Meniere's disease by administration of the compounds of the invention, and SR 121463A is a claimed embodiment administered for treating a disease in which vasopressin receptor is involved.

One would have been motivated to administer SR 121463A to a patient in need to treat Meniere's disease, as Foulon teaches that one could administer any compound of the invention or the salts to treat any disease in which vasopressin receptor is involved.

One would have had a reasonable expectation for success in treating Meniere's disease with SR 121463A, as Foulon teaches that one could administer any compound of the invention or the salts, and provides guidance on

the dosages to be administered and the routes of administration, to treat any disease in which vasopressin receptor is involved, including Meniere's disease.

With regards to the concentrations of the active element in the formulation administered (claims 16, 21 and 22), it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. concentration of the active ingredient in the formulation/medicament), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation, as Foulon teaches the dosages that can be formulated, *supra*. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

RESPONSE

Applicants respectfully traverse the rejection of claims 1-6, 9, 12-16, 21, and 22. Claims 2 and 3 have been cancelled and their subject matter added to claim 1. Therefore, the present rejection only applies to presently pending claims 1, 4-6, 9, 12-16, 21, and 22. The Examiner has failed to establish a *prima facie* case of obviousness against the presently rejected claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference. *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Applicants acknowledge, in the second full paragraph on page 2 of the instant application (English version), that the existence of vasopressin has been detected in the inner ear and that there was a suspected link in the prior art between vasopressin and disturbances/illnesses of the inner ear. However, the effect/activity of vasopressin in the inner ear was not known at the priority date of the present application. Also, the nature of the vasopressin receptor being present in certain parts of the inner ear was not known. It was the

inventors of the present application whom answered these questions.

Only the inventors of the present application could prove for the first time that:

1. vasopressin causes endolymphatic hydrops directly in the inner ear (*See* experiment 1 of the present invention);
2. the vasopressin receptor present in the endolymphatic sac is a V_2 receptor (*See* experiment 2 of the present invention); and
3. the activity of vasopressin is hindered by the addition of selective vasopressin-V_2-receptor antagonists and as a consequence the unwelcome hydrops can be positively influenced (*See* experiments 4 and 5 of the present invention).

Only these results of the inventors of the instant application obtained directly at the inner ear could show a person skilled in the art that vasopressin-V_2-receptor antagonists are useful for the treatment of disturbances or illnesses of the inner ear. It is under these preconditions that the art cited by the examiner has to be evaluated.

In this context, it is evidence that *Foulon* (WO 97/15556 A1) only discloses chemical compounds as well as their preparation. There is no concrete hint that such compounds can

be used for treatment or disturbances/illnesses of the inner ear. As a consequence, there are also no examples of any use of the compounds disclosed in *Foulon*. There is only a very general listing of a huge amount of totally different conditions for which these compounds are allegedly effective. However, there is no proof of the efficacy of the disclosed compound in the treatment of these conditions. As a consequence, the corresponding disclosure of *Foulon* is merely theoretical.

Therefore, a scientist practicing the invention in *Foulon* would not have a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made as required by *Amgen Inc.* A skilled artesian would not have thought of using vasopressin-V_2-receptor antagonists to positively influence unwelcome hydrops in the inner ear based on the disclosure of *Foulon*.

Further, *Serradeail-Le Gal* cannot add anything to the disclosure of *Foulon* or remedy its deficiencies. Otherwise, *Serradeail-Le Gal* deals with specific vasopressin-V_2-receptor antagonist SR 121463, however, the reference does not teach any link between this compound and disturbances/illnesses of the inner ear. Therefore, *Serradeail-Le Gal* fails as a reference for the same reason as *Foulon*.

Further, *In re Fine* requires some suggestion or incentive that would have motivated the skilled artisan to modify a reference. There is no motivation to combine *Foulon* with *Serradeail-Le Gal* to come up with the invention of the instant application because neither reference specifically teaches using a vasopressin-V_2-receptor antagonist to treat a disturbance or illness of the inner ear which is linked with an endolyphatic hydrop.

In conclusion, applicants identified the vasopressin-V_2-receptor (directly) in the inner ear and made available such receptor for the treatment with selective vasopressin-V_2-receptor antagonists as now claimed in amended claim 1.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of presently pending claims 1, 4-6, 9, 12-16, 21, and 22.

CONCLUSION

Based upon the above amendments and remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. Moreover, the Examiner is respectfully requested to reconsider and withdraw the rejections of pending claims 1, 4, 6-16, and 21-22.

The Examiner is welcomed to telephone the undersigned attorney if he has any questions or comments.

Respectfully submitted,

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